| ATENT COOPERA | JOH WOOD WO |
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| To: Edwards & Angell, LLP Attn. Alexander, John B. P.O. Box 9169 Boston, MA 02209 UNITED STATES OF AMERICA EDWARDS & ANGEL IP DOCKETING DEP | (PCT Rule 44.1) |
| Applicant's or agent's file reference | (day/month/year) 07/05/2004 |
| 60425 PCT | FOR FURTHER ACTION See paragraphs 1 and 4 below |
| International application No. | International filing date (day/month/year) 12/12/2003 |
| PCT/US 03/39607 Applicant | 12, 22, 2000 |
| Previous NEUROGEN CORPORATION | ly Docketed |
| NEUROGEN CORPORATION | |
| The applicant is hereby notified that the International Search Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claim When? The time limit for filing such amendments is norma International Search Report; however, for more de | s of the International Application (see Rule 46): |
| 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41–22) 740.14.35 | |
| For more detailed instructions, see the notes on the accordance | mpanying sheet. |
| 2. The applicant is hereby notified that no International Search Article 17(2)(a) to that effect is transmitted herewith. | Report will be established and that the declaration under |
| 3. With regard to the protest against payment of (an) addition | nal fee(s) under Rule 40.2, the applicant is notified that: |
| the protest together with the decision thereon has been | n transmitted to the International Bureau together with the lest and the decision thereon to the designated Offices. |
| no decision has been made yet on the protest; the app | olicant will be notified as soon as a decision is made. |
| 4. Further action(s): The applicant is reminded of the following: | |
| Shortly after 18 months from the priority date, the international application wishes to avoid or postpone publication, a notice priority claim, must reach the International Bureau as provided completion of the technical preparations for international publications. | e of withdrawal of the international application, or of the in Rules 90 <i>bis.</i> 1 and 90 <i>bis.</i> 3, respectively, before the |
| Within 19 months from the priority date, a demand for internation wishes to postpone the entry into the national phase until 30 mg | al preliminary examination must be filed if the applicant onths from the priority date (in some Offices even later). |
| Within 20 months from the priority date, the applicant must perfor before all designated Offices which have not been elected in the priority date or could not be elected because they are not bound | rm the prescribed acts for entry into the national phase e demand or in a later election within 19 months from the |
| Name and mailing address of the International Searching Authority | Authorized officer |
| European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Federico Bonomelli |

Form PCT/ISA/220 (July 1998)

ACJUBA 60425WO (72021)

From the INTERNATIONAL SEARCHING AUTHORITY

To:
Edwards & Angell, LLP
Attn. Alexander, John B.
P.O. Box 9169
Boston, MA 02209
UNITED STATES OF AMERICA

SEE
OFFICE SIDE
NOTIFICATION OF THANSMITTAL OF THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

| Boston, MA 02209 UNITED STATES OF AMERICA | | (PCT Rule 44.1) |
|---|---------------------------------------|---|
| | RECEIVE MAY 1 2 200 | Date of mailing |
| Applicant's or agent's file reference 60425 PCT | EDWARDS & ANGEL IP DOCKETING DEPT. | FURTHER ACTION See paragraphs 1 and 4 below |
| International application No. PCT/US 03/39607 | | International filing date (day/month/year) 12/12/2003 |
| Applicant NEUROGEN CORPORATION | | |
| | | |

| 1. X | ine app | licant is nereby n | lottiled that the international Search Report has been established and is transmitted herewise |
|----------|---------------------------------|--|---|
| | Filing of The app | f amendments a licant is entitled, | and statement under Article 19: if he so wishes, to amend the claims of the International Application (see Rule 46): |
| ٠ | When? | The time limit for International Se | or filing such amendments is normally 2 months from the date of transmittal of the earch Report; however, for more details, see the notes on the accompanying sheet. |
| | Where? | Directly to the | International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41–22) 740.14.35 |
| | For mor | re detailed instr | uctions, see the notes on the accompanying sheet. |
| 2. | The app Article 1 | licant is hereby r 7(2)(a) to that ef | notified that no International Search Report will be established and that the declaration undefect is transmitted herewith. |
| з. 🔲 | With re | gard to the prot | est against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: |
| | the ap | e protest togethe plicant's request | r with the decision thereon has been transmitted to the International Bureau together with the to forward the texts of both the protest and the decision thereon to the designated Offices. |
| | no no | decision has be | en made yet on the protest; the applicant will be notified as soon as a decision is made. |
| 4. Fur | ther actio | n(s): The app | licant is reminded of the following: |
| lf D | the applic | ant wishes to aven. must reach the | the priority date, the international application will be published by the International Bureau. oid or postpone publication, a notice of withdrawal of the international application, or of the e International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the preparations for international publication. |
| Wit w | hin 19 mo ishes to p | nths from the prostpone the entry | ionity date, a demand for international preliminary examination must be filed if the applicant y into the national phase until 30 months from the priority date (in some Offices even later). |
| Wit b | hin 20 mo efore all d | nths from the presignated Offices | iority date, the applicant must perform the prescribed acts for entry into the national phase s which have not been elected in the demand or in a later election within 19 months from the |

Name and mailing address of the International Searching Authority

European Patent Office, P.B. 5818 Patentiaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

priority date or could not be elected because they are not bound by Chapter II.

Authorized officer

Federico Bonomelli

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international politication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- [Where originally there were 15 claims and after amendment of all claims there are 11]:
 "Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
 - *Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or *Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged.*
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

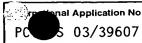
For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference | FOR FURTHER see Notification of (Form PCT/ISA/2 | of Transmittal of International Search Report 220) as well as, where applicable, item 5 below. |
|--|--|---|
| 60425 PCT International application No. | International filing date (day/month/year) | (Earliest) Priority Date (day/month/year) |
| PCT/US 03/39607 | 12/12/2003 | 13/12/2002 |
| Applicant | · | |
| NEURCISEN CORPORATION | 1 | |
| This international Search Report has been according to Article 18. A copy is being tra | n prepared by this International Searching Aut ansmitted to the International Bureau. | thority and is transmitted to the applicant |
| This International Search Report consists It is also accompanied by | of a total of sheets. a copy of each prior art document cited in this | s report. |
| Basis of the report | | |
| With regard to the language, the language in which it was filed, unline | international search was carried out on the ba less otherwise indicated under this item. | asis of the international application in the |
| the international search w Authority (Rule 23.1(b)). | vas carried out on the basis of a translation of | the international application furnished to this |
| b. With regard to any nucleotide ar was carried out on the basis of the | id/or amino acid sequence disclosed in the in equence listing: | nternational application, the international search |
| 1 | onal application in written form. | |
| | ernational application in computer readable for | m. |
| | this Authority in written form. | |
| | this Authority in computer readble form. | |
| international application a | bsequently furnished written sequence listing of as filed has been furnished. | |
| the statement that the inf furnished | ormation recorded in computer readable form ; | is identical to the written sequence listing has been |
| 2. X Certain claims were fou | ind unsearchable (See Box I). | |
| 3. Unity of invention is lac | king (see Box II). | |
| | | |
| 4. With regard to the title, | | |
| the text is approved as s | ubmitted by the applicant. | |
| 1 1 | shed by this Authority to read as follows: | |
| CARBOXYLIC ACID, PHOS ANALOGUES AS CAPSAICI | PHATE OR PHOSPHONATE SUBSTI' N RECEPTOR MODULATORS | TUTED QUINAZOLIN-4-YLAMINE |
| * | | |
| 5. With regard to the abstract, | | |
| | ubmitted by the applicant. | |
| the text has been establi within one month from the | shed, according to Rule 38.2(b), by this Autho e date of mailing of this international search re | ority as it appears in Box III. The applicant may, eport, submit comments to this Authority. |
| 6. The figure of the drawings to be put | olished with the abstract is Figure No. | |
| as suggested by the app | licant. | None of the figures. |
| because the applicant fa | iled to suggest a figure. | |
| because this figure bette | r characterizes the invention. | |

INTENATIONAL SEARCH REPORT



A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07D401/04 C07D471/04 C07F9/09 C07F9/38

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

| C. DOCUM | ENTS CONSIDERED TO BE RELEVANT | T |
|------------|--|-----------------------|
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| P,X | WO 03/062209 A (BAKTHAVATCHATAM RAJAGOPAL; BRIELMANN HARRY L (US); NEUROGEN CORP (US)) 31 July 2003 (2003-07-31) cited in the application the whole document | 1-73 |
| P,A | WO 03/049702 A (DOHERTY ELIZABETH M; NORMAN MARK HENRY (US); OGNYANOV VASSIL I (US);) 19 June 2003 (2003-06-19) claim 21; example 118 | 1-73 |
| P,A | WO 03/099284 A (DOHERTY ELIZABETH M; AMGEN INC (US); CHEN NING (US); NORMAN MARK H (U) 4 December 2003 (2003-12-04) claim 1; examples 10,11 | 1-73 |
| | -/ | |
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| Further documents are listed in the continuation of box C. | χ Patent family members are listed in annex. |
|---|---|
| Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but tater than the priority date claimed | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family |
| Date of the actual completion of the international search | Date of mailing of the international search report |
| 29 April 2004 | 07/05/2004 |
| Name and mailing address of the ISA | Authorized officer |
| European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Von Daacke, A |

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| C.(Continua | ation) DOCUMENTS CONSIDERED TO BE RELEVANT | |
|-------------|--|-----------------------|
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | WO 02/08221 A (BAKTHAVATCHALAM RAJAGOPAL; DESIMONE ROBERT W (US); NEUROGEN CORP (US)) 31 January 2002 (2002-01-31) claim 1; examples 38-42,102-106 | 1-73 |
| A | EP 0 652 218 A (TAKEDA CHEMICAL INDUSTRIES LTD) 10 May 1995 (1995-05-10) example 74 | 1-73 |
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| ١ | Box I | Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) | |
|---|-----------|--|-----|
| • | This Inte | ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: | |
| | 1. X | Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: | |
| | | Although claims $33-59,61,62$ AND $67-73$ are directed to a method of treatment the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. | of |
| | 2. | Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: | |
| | | | , |
| | | | |
| | 3 | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). | |
| | Box II | Observations where unity of invention is lacking (Continuation of item 2 of first sheet) | |
| | This Inte | ernational Searching Authority found multiple inventions in this international application, as follows: | |
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| | 1. | As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. | |
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| | 2. | As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. | |
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| | | No. of the second secon | |
| | 3. | As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: | ÷ |
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| | 4. | No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: | |
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| | | | ٠. |
| | Remark | k on Protest | |
| 1 | | | |
| | | No protest accompanied the payment of additional search fees. | |

INTERNATIONAL SEARCH REPORT

mation on patent family members

PCS 03/39607

| P | atent document | | Publication | | Patent family | | Publication |
|----|--------------------|-------|-------------|--------|---------------------|-----|--------------------------|
| | d in search report | 1 | date | | member(s) | | date |
| WO | 03062209 | Α | 31-07-2003 | WO | 03062209 | A2 | 31-07-2003 |
| WO | 03049702 | A | 19-06-2003 | WO | 03049702 | | 19-06-2003 |
| | | | | US | 2003195201 | | 16-10-2003 |
| | | | | WO | 03099284 | | 04-12-2003 |
| | | | | US | 2004038969 | | 26-02-2004 |
| | | | | WO | 2004014871 | | 19-02-2004 |
| WO | 03099284 | Α | 04-12-2003 | WO | 03049702 | | 19-06-2003 |
| | | | | WO | 03099284 | | 04-12-2003 |
| | | | | US | 2003195201 | | 16-10-2003 |
| | | | | US | 2004038969 | A1 | .26-02-2004 |
| WO | 0208221 | Α | 31-01-2002 | AU | 8066701 | | 05-02-2002 |
| | | | | BR | 0112631 | | 23-09-2003 |
| | | | | CA | 2415606 | | 31-01-2002 |
| | | | 4. | CN | 1443170 | | 17-09-2003 |
| | | | | EP | 1301484 | | 16-04-2003 |
| | | | | WO | 0208221 | | 31-01-2002 |
| | | · | · | US | 2002132853 | A1 | 19-09-2002 |
| ΕP | 0652218 | Α | 10-05-1995 | AT | 203024 | | 15-07-2001 |
| | | | | AU | 678295 | | 22-05-1997 |
| | | | | ΑU | 7773894 | | 18-05-1995 |
| | | | | BR | 9404403 | | 18-07-1995 11-05-1995 |
| | | | | CA | 2135440 | | 30-08-1995 |
| | | | | CN | 1107476 69427675 | D1 | 16-08-2001 |
| | | | | DE | 69427675 | | 16-05-2002 |
| | | | • | EP | 0652218 | | 10-05-1995 |
| | | | | FI | 945281 | | 11-05-1995 |
| | | | | ห่บ้ | 68810 | | 19-05-1995 |
| | • | • | | JP | 8067678 | | 12-03-1996 |
| | | • | | NO | 944252 | | 11-05-1995 |
| | | | | NZ | 264887 | | 20-12-1996 |
| | | | | NZ | 272711 | Α | 29-06-1999 |
| - | | | • | RU | 2135471 | | 27-08-1999 |
| | | V | | US | 5585385 | | 17-12-1996 |
| | (5) | | | BR | 9501976 | Α . | 30-04-1996 |